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**[54] INHIBITION OF SELECTIN BINDING**

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[\*] Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

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- [51] **Int. Cl.**<sup>6</sup> A61K 31/70; G01N 33/53
- [52] **U.S. Cl.** ..... 514/25; 514/42; 514/53; 514/54; 514/61; 435/7.1; 435/7.2
- [58] **Field of Search** ..... 514/25, 42, 53, 514/54, 61; 435/7.1, 7.2

**[56] References Cited****U.S. PATENT DOCUMENTS**

5,512,294 4/1996 Li et al. ..... 424/450

**OTHER PUBLICATIONS**

- Harlow et al. Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988.
- Pearce el al. Molecular Microbiology 9(5):1037-50, 1993.
- Yother et al. Journal of Bacteriology 174(2): 610-618, 1992.
- Talkington et al. Microbiol Pathogenesis 13: 343-355, 1992.
- Andersson et al., Microbial Pathogenesis 4:267-78, 1988.
- Pearce et al., 1994, Molec. Microbiol. 12:881-92.
- Geelen et al., 1993, Infect. Immun. 61:1538-1543.
- Park, 1993, J Bacteriol. 175:7-11.
- Ruhfel et al. 1993, J. Bacteriol. 175:5253-59.
- Tanimoto et al., 1993 J. Bacteriol. 175:5260-4.
- Pearce et al., 1993, Mol. Microbiol. 9:1037-50.
- Trombe, 1993, J. Gen. Microbiol. 139:433-9.
- Wang et al., 1993, Proc. Natl. Acad. Sci. USA 90:4156-60.
- Hoepelman and Tuomanen, 1992, Infect. Immun. 60:1729-33.
- Jenkinson, 1992, Infect. Immun. 60:1225-8.
- Martin et al., 1992, EMBO J. 11:3831-6.
- Martin et al., 1992, J. Bacteriol. 174:4517-4523.

Pearce and Masure, 1992, Abstr. Gen. Meet. Am. Soc. Microbiol. 92:127, D-188.

Perez-Martinez et al., 1992, Mol. Gen. Genet. 234:401-11.

Saier and Reizer, 1992, J. Bacteriol. 174:1433-1448.

Schmid and Linder, 1992, Mol. Microbiol. 6:283-92.

Squires and Squires, 1992, J. Bacteriol. 174:1081-5.

Taha et al., 1992, J. Bacteriol. 174:5978-81.

Talkington et al., 1992, Microb. Pathog. 13:343-55.

Tang et al., 1992, Nature 356:152-54.

Yother et al., 1992, J. Bacteriol. 174:610-8.

Gonzy-Tréboul et al., 1991, Mol. Microbiol. 5:1241-9.

Payne and Jackson, 1991, J. Bacteriol. 173:2278-82.

Snavely et al., 1991, J. Biol. Chem. 266:815-23.

Toone et al., 1991, J. Bacteriol. 173:3291-3302.

Alloing et al., 1990, Mol. Microbiol. 4:633-44.

Gottesman et al., 1990, Proc. Natl. Acad. Sci. USA 87:3513-7.

Holmberg et al., 1990, J. Gen. Microbiol. 136:2367-75.

Alloing et al., 1989, Gene 76:363-8.

Gutierrez and Devedjian, 1989, Nucleic Acid Res. 17:3999.

Andersson et al., 1988, Microb. Pathogen. 4:267-278.

Chen and Morrison, 1988, Gene 64:155-64.

Gilson et al., 1988, EMBO J. 7:3971-4.

Glaser et al., 1988, Mol. Microbiol. 2:19-30.

Glaser et al., 1988, EMBO J. 7:3997-4004.

Smith et al., 1988, Gene 70:351-61.

Taha et al., 1988, EMBO J. 7:4367-78.

Smith et al., 1987, J. Bacteriol. 169:3321-28.

Hoffman and Wright, 1985, Proc. Natl. Acad. Sci. U.S.A. 82:5107-11.

Manoil and Beckwith, 1985, Proc. Natl. Acad. Sci. U.S.A. 82:8129-33.

Beachey, 1981, J. Inf. Diseases 143:325.

Tiraby and Fox, 1973, Proc. Natl. Acad. Sci. U.S.A. 70:3541-3545.

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**[57] ABSTRACT**

This invention provides a system for inhibiting the binding between two cells, one expressing P- or L-selectin on the surface and the other expressing the corresponding ligand. A covalently crosslinked lipid composition is prepared having saccharides and acidic group on separate lipids. The composition is then interposed between the cells so as to inhibit binding. Inhibition can be achieved at an effective oligosaccharide concentration as low as 10<sup>6</sup> fold below that of the free saccharide. Since selectins are involved in recruiting cells to sites of injury, this system can be used to palliate certain inflammatory and immunological conditions.

**38 Claims, 8 Drawing Sheets**